A STUDY OF HAEMOPHILIC PATIENT'S INDICATION FOR ADMISSION AND EARLY DETCTION OF ARTHROPATHY

Dissertation submitted in partial fulfillment of regulation for the award of M.D. Degree in General Medicine (Branch I)

The Tamilnadu DR. M.G.R. Medical University
April 2012

Certificate

Certified that this is the bonafide dissertation done by ***Dr. UNNIKRISHNAN.S.*** *and submitted in partial fulfillment of the requirements for the Degree of M.D., General Medicine, Branch I of The Tamilnadu DR. M.G.R. Medical University, Chennai.*

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DECLARATION

I solemnly declare that the dissertation titled

"A STUDY OF HAEMOPHILIC PATIENT'S INDICATION FOR ADMISSION AND EARLY DETCTION OF ARTHROPATHY"

was done by me from June 2010 to october 2011 under the guidance and supervision of Professor **Dr.S.USHA.MD.**

This dissertation is submitted to the Tamilnadu DR. MGR Medical University towards the partial fulfillment of the requirement for the award of MD

Degree in General Medicine (Branch I).

Dr.UNNIKRISHNAN.S.

Place: Coimbatore
Date: 05.12.2011

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CONTENTS

ABSTRACT

Haemophilia is a disorder of coagulation. Haemophilia A is due to deficiency of clotting factor VIII and haemophilia B is due to deficiency of factor IX. Both are inherited as X-linked, so males usually exhibit the disease and females are carriers. Prevalence of haemophilia A is 1 in 5,000 to 10,000 male births and that of haemophilia B is 1 in 20,000 to 34,000 births. Haemophilia A accounts for about 80% cases of haemophilia and haemophilia B around 20%. Arthropathy is a common and debilitating complication of haemophilia. If detected earlier progression of disease process can be arrested by effective management.

METHODS

Here 40 patients with haemophilia are studied and their indications of admissions were noted. They were assessed clinically as well as radiologically for the detection of arthropathy irrespective of whether they were admitted for musculoskeletal bleeds or not.

RESULTS

Majority of patients were admitted with musculoskeletal bleeds(29 of 40). Most of the patients were haemophilia A patients(34 of 40). Family history was

present in only 10% cases. Majority of patients(23 of 40) were in stage III of haemophilic arthropathy as staged according to Arnold hilgartner classification. Out of 11 patients admitted with non musculoskeletal bleeds only one had clinical evidence of arthropathy and out of the remaining 10 patients 4 were already in stage III of haemophilic arthropathy without any symptoms and signs. Arthropathy worsens as the duration of disease process increases.

CONCLUSIONS

Haemophilia is a common coagulation disorder encountered by physicians. The most common indication for admissions are musculoskeletal bleeds and knee being the commonest joint involved. As the duration of disease process increases the risk of permanent joint damage also goes on the increase. Those patients with early stages of arthropathy are treated conservatively with factor replacement therapy to halt the progression of disease. If not treated adequately, due to chronic synovitis permanent joint damage occurs. Once this happens only surgical cure is possible to restore the joint function. The various modalities available are synovectomy, arthroplasty and joint replacement in severe cases.

Even in haemophilics admitted for non-musculoskeletal indications arthropathy may lie undetected and if unnoticed can result in joint damage.

INTRODUCTION

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Haemophilia is a disorder of coagulation. Haemophilia A is due to deficiency of clotting factor VIII and haemophilia B is due to deficiency of factor IX. Both are inherited as X-linked, so males usually exhibit the disease and females are carriers.

Prevalence of haemophilia A is 1 in 5,000 to 10,000 male births and that of haemophilia B is 1 in 20,000 to 34,000 births. Haemophilia A accounts for about 80% cases of haemophilia and haemophilia B around 20%. Haemophilia C is due to deficiency of factor XI and unlike other haemophilias it is autosomal and is also the rarest of the three.

Haemophilia lowers blood plasma clotting factor levels of the coagulation factors needed for a normal clotting process. Thus when a blood vessel is injured, a temporary scab does form, but the missing coagulation factors prevent fibrin formation, which is necessary to maintain the blood clot. A haemophiliac does not bleed more intensely than a person without it, but can bleed for a much longer time. In severe haemophiliacs even a minor injury can result in blood loss lasting

days or weeks, or even never healing completely. In areas such as the brain or inside joints, this can be fatal or permanently debilitating.

Spontaneous and recurrent haemarthrosis can lead to a deforming arthritis. Chronic arthritis can result in restricted joint motion, or laxity with subluxation, features of end stage disease. In patients with chronic symptomatic synovial proliferation and recurrent haemarthrosis, synovectomy is beneficial rather than conservative management useful in early stages of disease.

So early detection of arthropathy and surgical intervention can improve the quality of life of these patients with drastic reduction in both mortality and morbidity.

AIM OF STUDY

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- To find out the indications for admission of haemophilia patients

- Early detection of haemophilic arthropathy, clinically and radiologically

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Haemophilia refers to a group of inherited diseases in which there is a functional deficiency of a specific clotting factor. The most common are hemophilia A(classic hemophilia)and hemophilia B (Christmas disease); the deficient factors are factor VIII (hemophilia A) and factor IX (hemophilia B). The incidence and severity of hemorrhagic complications of hemophilia are directly related to the severity of the underlying coagulation defect.

Although the intrinsic pathway of coagulation is severely impaired in hemophilia, the extrinsic tissue factor -dependent pathway remains intact and is probably the major hemostatic regulatory system. Normal synovial tissue and cultures of synovial fibroblasts have been found to be deficient in tissue factor, [2] which suggests that in synovium-lined joints, hemophiliacs have functional inactivity of intrinsic and extrinsic coagulation pathways. This situation may explain the marked propensity toward hemorrhage in joints compared with other tissue sites in these patients.

CLINICAL FEATURES

Distribution of acute haemarthrosis based on a study of 139 patients with hemophilia by *Steven MM, Yogarojah S, Madhok R, et al: Haemophilic arthritis. QJM 58:181, 1986.)*

Percentage joints with:

Any hemarthrosis	Many hemarthroses	Chronic pain	Synovitis	Limitation of motion	Any radiologic abnormality
34.5	13.3	13.9	—	16.9	21.6
54.0	38.5	13.8	9.8	27.0	52.6
28.6	8.0	5.4	—	19.8	18.8
63.1	50.9	26.8	11.6	27.0	50.2
60.8	42.8	15.2	2.2	34.2	52.4

ACUTE HEMARTHROSIS

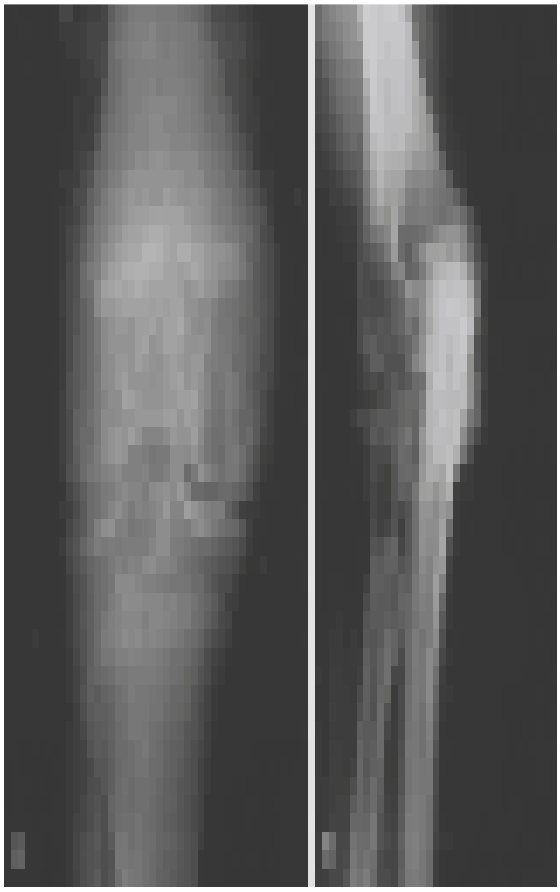
Nearly all patients with severe hemophilia A or B (<1% activity of the deficient factor) and half of patients with moderate disease activity experience haemarthrosis. Acute hemarthroses generally first occur when a child begins to walk and continue, usually cyclically, into adulthood, when the frequency diminishes. Patients frequently have premonitory symptoms, such as stiffness

or warmth in the affected joint, followed by intense pain, which may be due partly to rapid joint capsule distention.

Pain is accompanied by objective clinical findings of warmth, a tense effusion, tenderness, limitation of motion, and a joint that is often held in a flexed position. Joint pain responds rapidly to replacement of the deficient clotting factor. If hemostasis is achieved early after onset of haemarthrosis, full joint function may be regained within 12 to 24 hours. If the hemorrhage is more advanced, however, blood is resorbed slowly over 5 to 7 days, and full joint function is regained within 10 to 14 days.

SUBACUTE OR CHRONIC ARTHRITIS

Recurrent hemarthroses, particularly in patients with severe factor deficiency, may lead to a self-perpetuating condition in which joint abnormalities persist in intervals between bleeding episodes. The involved joint is chronically swollen, although painless and only slightly warm. Chronic synovitis, including prominent synovial proliferation with or without effusion, may be present. There may be mild limitation of motion, often with a flexion deformity. Factor replacement does not modify these findings.

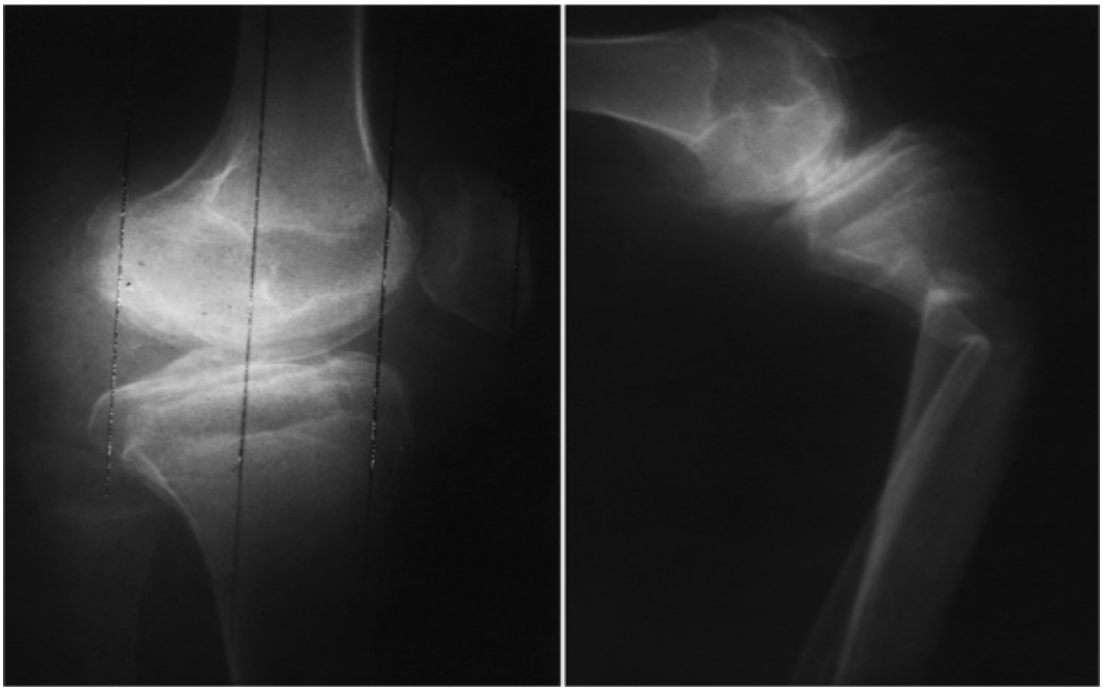


Radiographic changes of hemophilic arthropathy. **A,** Early arthritis of the knee, showing soft tissue swelling, widening of the femoral condyles and tibial plateau, irregularity of the distal femoral epiphysis, and a few subchondral bone cysts. **B,** More advanced arthritis involving the elbow, showing almost complete loss of joint space and extensive subchondral cyst formation. The widening of the proximal radius is characteristic of hemophilic arthropathy.

END-STAGE HEMOPHILIC ARTHROPATHY

Long-standing end-stage hemophilic arthropathy has features in common with degenerative joint disease and advanced rheumatoid arthritis. The joint appears enlarged and "knobby," owing to osteophytic bone overgrowth. Synovial thickening and effusion are not prominent, however. Range of motion is severely restricted, and fibrous ankylosis is common. Subluxation, joint laxity,

and malalignment are frequently present. Hemarthroses decrease in frequency, however.



SEPTIC ARTHRITIS

Until the early 1980s, septic arthritis rarely occurred in hemophiliac patients. With the widespread occurrence of human immunodeficiency virus (HIV) infection as a result of contaminated factor concentrates, the incidence of this complication has increased significantly.[3,4] Septic arthritis is seen more often in adult than in pediatric hemophiliacs and is most commonly monoarticular, usually involving the knee. In contrast to spontaneous haemarthrosis, septic

arthritis is significantly associated with a temperature greater than 38oC within 12 hours of presentation and articular pain that does not improve with replacement therapy.[3] Peripheral leukocyte count may not be elevated, particularly in HIV-positive patients.[5] A predisposing factor other than hemophilic arthropathy is often identifiable, including previous arthrocentesis or arthroplasty, intravenous drug use, and infected indwelling venous access catheters. *Staphylococcus aureus* is the most frequently identified organism even in HIV-infected patients, followed by *Streptococcus pneumoniae*.[5]

MUSCLE AND SOFT TISSUE HEMORRHAGE

Bleeding into muscles and soft tissue is common in hemophiliacs and may be more insidious than haemarthrosis because of the lack of premonitory symptoms. Bleeding into the iliopsoas and gastrocnemius muscles and the forearm results in well-described syndromes with which the rheumatologist should be familiar. Iliopsoas hemorrhage produces acute groin pain with marked pain on hip extension and a hip flexion contracture. Rotation is preserved, in contrast to intra-articular hemorrhage. If untreated, the expanding soft tissue mass may compress the femoral nerve, causing signs and symptoms of femoral neuropathy.[6, 7] Bleeding into the gastrocnemius muscle can cause an equinus deformity from heel cord contracture.[6] Finally, hemorrhage into closed compartments can cause acute muscle necrosis and nerve

compression.[8] Of particular importance is bleeding into the volar compartment of the forearm, which can cause flexion deformities of the wrist and fingers. If a compartment syndrome is suspected, compartment pressures should be measured to confirm the diagnosis.

A large intramuscular hemorrhage uncommonly results in the formation of a simple muscle cyst, which clinically appears to be an encapsulated soft tissue area of swelling overlying muscle. Cyst formation in this setting is confined by the muscular fascial plane and most likely results from inadequate resorption of blood and clot. Subperiosteal or intraosseous hemorrhage, in contrast, may lead to a pseudotumor, a rare skeletal complication of hemophilia. Hemophilic pseudotumors are of two types: the adult type, which occurs proximally, usually in the pelvis or femur; and the childhood type, which occurs distal to the elbows or knees and carries a better prognosis.[9, 10]

Conservative early management of muscle cysts and childhood-type pseudotumors is indicated, including immobilization and factor replacement. In adult-type pseudotumors, which are usually refractory to conservative therapy, and in progressive childhood pseudotumors, surgical removal is indicated[9] to prevent serious complications, such as spontaneous rupture, fistula formation, neurologic or vascular entrapment, and fracture of adjacent bone. Aspiration of a pseudotumor or cyst is contraindicated.

DIAGNOSTIC IMAGING

RADIOGRAPHS

The earliest radiographic changes in hemophilic arthropathy are confined to the soft tissue and reflect acute haemarthrosis. The joint capsule is distended with displacement of fat pads, and there is an increased hazy density caused by intra-articular blood. Haemarthrosis before epiphyseal plate closure may result in epiphyseal overgrowth and irregularity. Occasionally, premature epiphyseal closure is seen.

With the progression of chronic proliferative synovitis, irreversible radiologic changes appear.[11] these changes reflect the inflammatory and the degenerative nature of chronic hemophilic arthropathy. A study of serial radiographs of symptomatic joints in hemophilic patients suggests that serial scoring with conventionally accepted techniques may be a cost-effective alternative to magnetic resonance imaging (MRI) in predicting progressive synovial hypertrophy.[12]

Radiologic Manifestations of Chronic Hemophilic Arthropathy

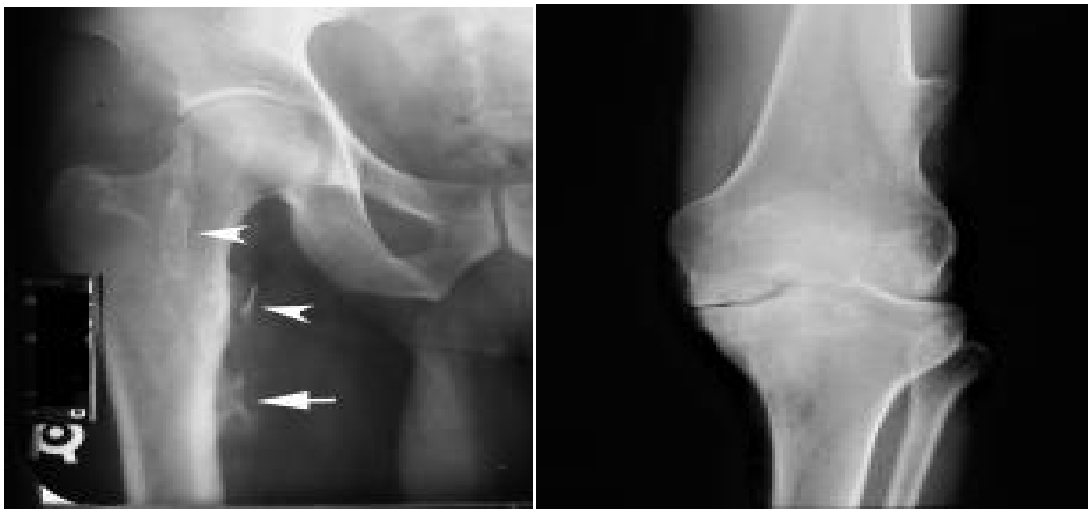
Characteristic	Also Seen in

Characteristic	Also Seen in
Periarticular soft tissue swelling	RA
Periarticular demineralization	RA
Marginal erosions	RA
Subchondral irregularity and cyst formation	RA, OA
Decreased joint space	OA
Osteophyte formation	CPPD[*]
Chondrocalcinosis	
Specific Femoral intercondylar notch widening Squaring of distal patellar margin (lateral view) Proximal radial enlargement Talar flattening? ankle ankylosis[†]	

CPPD, calcium pyrophosphate deposition disease; OA, osteoarthritis; RA, rheumatoid arthritis.

* From Jensen PS, Putnam CE: Chondrocalcinosis and hemophilia. Clin Radiol 28:401, 1977.

† From Schreiber RR: Musculoskeletal system: Radiologic findings. In Brinkhous KM, Hemker HC (eds): Handbook of Hemophilia, I. New York, American Elsevier, 1975.



OTHER IMAGING METHODS

MRI is now routinely used to stage hemophilic arthritis accurately to determine optimal treatment and to follow response to therapy.[13]A scoring system based on MRI has been proposed.[14] Additionally, MRI and ultrasonography are useful in the detection and the quantitation of soft tissue bleeding, cysts, and pseudotumors.

MRI image in a patient with hemophilic arthropathy shows dark, synovial masses that erode the cartilage and produce subchondral cysts

PATHOLOGIC FEATURES AND PATHOGENESIS

Pathologic studies of human hemophilic arthropathy have been limited to synovial specimens obtained at surgery[15, 16] or at postmortem examination and reflect changes of advanced disease only. Studies of experimentally produced haemarthrosis in animals, [17, 18] post-traumatic haemarthrosis in nonhemophilic humans, [19] and canine and murine models of hemophilia A[20-22] have provided an understanding of the earliest changes induced by acute haemarthrosis and their evolution to chronic arthritis.

As reviewed more recently, [23] the process most likely includes catabolic activation of synovial cells by exposure to blood components with subsequent

cartilage destruction and a direct destructive effect of intra-articular blood on cartilage. A single synovial hemorrhage induces serial changes in the synovial membrane, including early focal villous synovial proliferation and subsynovial diapedesis of erythrocytes, followed by the appearance of perivascular inflammatory cells, patchy subsynovial fibrosis, and intracellular iron accumulation in synovial cells and subsynovial macrophages. With repeated hemarthroses, the synovium becomes grossly hypertrophied and hyperpigmented, with eventual organization into a pannus that invades and erodes marginal cartilage. On histologic examination, villous hypertrophy and subsynovial fibrosis progress, but inflammatory cells are scarce.[16] Seventy-five percent of synoviocytes contain siderosomes (electron-dense, iron-filled deposits within lysosomes), in contrast to 10% in normal synovium and 25% in rheumatoid synovium.[24] Iron deposits are associated with the production of proinflammatory cytokines and synovial inhibition of the formation of human cartilage matrix. Although the inflammatory synovial changes are mild, the synovial production of proinflammatory mediators, including interleukin-1 and interleukin-6 and tumor necrosis factor-α, approaches that of rheumatoid synovium.[23] The articular cartilage is grossly and microscopically abnormal in the setting of recurrent hemarthrosis.[17] There are areas of cartilaginous fissuring and rarefaction exposing sclerotic bone. The remaining cartilage is

thin and unevenly distributed, often freely protruding into the joint cavity. Bone erosions appear at weight-bearing surfaces. There is loss of matrix glycosaminoglycan, which also is seen in degenerative arthritis.[16, 25]

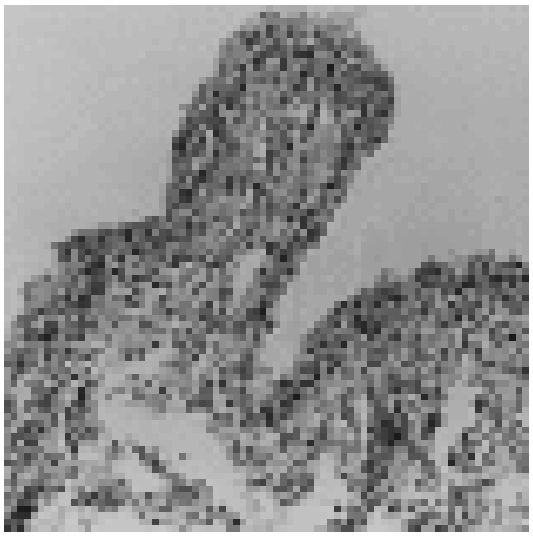


Figure. Proliferative synovitis of hemophilia. Villous hypertrophy of synovium with pigment deposition in superficial cells. The reaction is mainly synovial cell hyperplasia. Infiltrating inflammatory cells are scarce (Hematoxylin and eosin).

Current studies suggest that recurrent haemarthrosis induces joint destruction in hemophilic arthropathy through direct and indirect effects of iron on the synovium[24,26] and cartilage,[25,27] by the degradative effect of the proliferative synovium, and through an alteration in cartilage biochemical composition similar to that seen in degenerative arthritis. There may be a relationship between haemarthrosis-induced overexpression of oncogenes (e.g., *c-myc* and *mdm-2*) and the dysregulated, tumor-like proliferation of hemophilic synovium.[29, 30]

DIAGNOSIS

In most cases of congenital coagulopathy, the diagnosis has been made before presentation to a rheumatologist. In the case of hemophilia, if there is an affected family member, prenatal diagnosis is possible. Because the spontaneous mutation rate in hemophilia is significant, the diagnosis may not be suspected until infancy, when recurrent, large ecchymoses or sustained oral hemorrhages commonly develop in most affected patients. In the case of hemophilia A or hemophilia B, haemarthrosis is usually a later manifestation, but it may be the initial symptom of other, less severe coagulopathies, even in adulthood. When a coagulopathy is suspected, baseline screening tests, including prothrombin time, activated partial thromboplastin time, and platelet count, should be performed. In patients with hemophilia, the prothrombin time and platelet count are normal, and the activated partial thromboplastin time is prolonged, denoting a defect in the intrinsic clotting cascade. Referral to a hematologist, who obtains the appropriate factor assays, is the next step.

Individuals with factor VIII or IX levels of 1% or less of the normal level have joint and muscle hemorrhages requiring therapy on an average four or five times per month. Such patients are classified as having severe hemophilia. Individuals with factor VIII or IX levels greater than 5% of normal are considered to have mild hemophilia and usually bleed only with trauma or at

surgery. Occasional “spontaneous” haemarthrosis may occur in such patients, especially in joints damaged by previously undertreated hemorrhage.

Patients whose factor VIII or IX levels fall between these two ranges are considered to have moderately severe hemophilia, and their clinical picture falls somewhere between the extremes. If such patients have had multiple untreated or suboptimally treated hemarthroses with subsequent joint damage, the anatomic instability of these joints would cause frequent and severe bleeding, and the condition would appear clinically more severe than the factor VIII or IX assay might suggest.

TREATMENT OF HEMOPHILIA

Until recent years, in most hemophilia centers factor replacement therapy has been given on demand; that is, factor concentrate has been infused at the earliest sign of a hemorrhage. With the introduction of highly purified, safe concentrates, prophylactic treatment is now much more common in countries where this product is available, especially in pediatric patients.[31,32]Instead of being infused when a hemorrhage has occurred, factor concentrate is given regularly three times per week to prevent bleeds. Prophylaxis is started before any joint damage has occurred, usually at approximately 2 years of age, with the goal of minimizing bleeding episodes to no more than four to six per year.

Indwelling catheters, such as Port-A-Cath and Hickman lines, are required for factor administration because frequent venipunctures are painful and cumbersome. More recent data suggest that the institution of prophylactic factor infusion would significantly decrease the long-term joint sequelae of hemophilia and decrease lifetime disability.[33, 34, 35]

With adequate factor replacement, all types of surgery, including joint replacements, can be done. Surgical intervention in a patient with hemophilia should be done, however, only at specialized centers with blood bank and coagulation laboratory support and with the participation of a hematologist who specializes in clotting disorders. A surgeon who feels comfortable operating on patients with clotting disorders also is essential. Constant-infusion techniques for administering factor concentrate during and after surgery have made adequate factor levels easier to maintain and have decreased overall perioperative use of factor concentrates.[36] Many types of commercial factor VIII concentrate are available, most of which are manufactured with recombinant technology.

FACTOR VIII REPLACEMENT

All plasma-derived factor concentrates are virally inactivated by various methods, including exposure to solvent detergent, heat, and pasteurization.

Recombinant factor VIII concentrates, manufactured by inserting the human factor VIII gene into a mammalian cell line, are widely available and used almost exclusively, especially in developed countiries.[37, 38] Because human plasma is not used in their production, transfusion-transmitted diseases, such as hepatitis and HIV-1, are no longer a risk. Recombinant concentrates at doses similar to those of plasma-derived concentrates have been efficacious in the treatment of hemorrhages. Half-life and recovery times for the infused factor VIII are similar to those for plasma-derived concentrates. Current prices range from $0.35 to $0.90 per unit for factor VIII plasma-derived concentrates and from $1.00 to $1.20 per unit for recombinant factor VIII. In most hemophilia centers in the United States, recombinant factor concentrates are the only concentrates used, although high-purity, plasma-derived concentrates are still available. Because these concentrates have made early and intensive home therapy possible, overall costs of health care have greatly declined for patients treated with these materials.

Arginine vasopressin (desmopressin), a vasopressin analogue, can be used in the treatment of mild hemophilia A to increase the endogenous factor VIII level. Desmopressin increases the baseline factor VIII level about threefold, so a baseline level of at least 10% is required for efficacy.[39]Because this is not a blood product, it poses no danger of transmitting blood-borne viruses.

Although cryoprecipitate contains factor VIII, its use has been discouraged because it is not virally inactivated. It is less safe than concentrates.

FACTOR IX REPLACEMENT

Factor IX is not found in either cryoprecipitate or factor VIII concentrate; these two materials are totally ineffective for the treatment of hemophilia B. Fresh-frozen plasma does contain factor IX and has been used in the past. Most fresh-frozen plasma products are not virally inactivated and are less safe than factor IX concentrates.

The principles of treatment are similar to those for factor VIII replacement. Because the half-life of factor IX is longer, however, it can be given less frequently. Demand therapy is still commonly used; as for factor VIII deficiency, however, prophylaxis is beginning to be used in pediatric patients. Several plasma-derived factor IX concentrates are available, all virally inactivated. In the past, all such concentrates also contained factors II, VII, and X (prothrombin complex concentrates). Currently, only pure factor IX concentrates are used to treat factor IX deficiency. As with factor VIII concentrates, a recombinant factor IX concentrate is available and is widely used. Recovery is less than that of its plasma-derived counterpart, however,

and higher doses (approximately 1.5 times calculated levels) must be infused to reach appropriate levels.

COMPLICATIONS OF FACTOR REPLACEMENT THERAPY

Inhibitor Antibodies

Inhibitor antibodies may develop after exposure to factor concentrate. They occur most often in patients with severe hemophilia after 9 to 30 exposures of replacement therapy, usually before the age of 5 years. There may be a familial predisposition to the development of this complication. Because bleeding cannot be reliably controlled in patients with inhibitor antibodies, elective surgery in these patients should be done only after careful deliberation.

Inhibitor antibodies in factor VIII–deficient hemophiliacs are IgG antibodies (usually IgG4) and may have an unpredictable natural history. Low titer and clinically weak antibodies sometimes are easily neutralized by factor VIII and do not undergo anamnestic increases in titer after multiple factor VIII challenges. Such antibodies may rarely become high in titer. In other patients, antibody titers increase after each exposure to factor VIII. Still other patients seem to lose antibody spontaneously despite multiple subsequent factor VIII challenges. The type of antibody response to factor VIII infusion and the patient's clinical response dictate therapy.

Therapy for patients with inhibitor antibodies have been reviewed more recently.[40] Induction of immune tolerance through frequent administration of factor VIII successfully eliminates inhibitors in 80% of patients. In patients in whom immune tolerance therapy is unsuccessful, there are several approaches for management of acute bleeding episodes, including the administration of activated prothrombin complex concentrate or, more recently, recombinant activated factor VIIa (rVIIa, Novo-Seven; Novo Nordisk, Bagsvaerd, Denmark). rVIIa is thought to function directly at the site of injury, causing activation of factor IX and the extrinsic clotting system locally. Porcine factor VIII, which has limited cross-reactivity with the human antibody, was used previously, but has been removed from the market because of contamination with porcine parvovirus. A recombinant form of this protein is being investigated.

The use of immunosuppressives or glucocorticoids has been abandoned in most centers owing to lack of efficacy in this condition and serious side effects. Regimens of regular factor VIII infusions for induction of tolerance have been successful in eliminating the antibody. It has been suggested by some groups that an immune tolerance regimen be started as early as possible after an inhibitor develops. Rituximab may be useful to suppress inhibitor titers in refractory patients.[41]

Inhibitor antibodies against factor IX are exceedingly rare. There is no generally accepted efficacious therapy. Treatment usually includes large and frequent doses of factor IX concentrate. Induction of immune tolerance with elimination of the antibody also has been used, but with less success than with antibodies to factor VIII. Using large doses of purified factor IX concentrate in some patients with inhibitor antibodies to factor IX has resulted in anaphylactic reactions and nephrotic syndrome secondary to immune complex formation and deposition in the kidney.[42, 43]

Human Immunodeficiency Virus

HIV was introduced into the U.S. blood supply in the 1970s. By the late 1970s, factor concentrate was widely contaminated. By 1982, approximately 50% of patients with hemophilia were infected with HIV.[44] Currently; approximately 10% to 20% of American hemophiliacs are infected with HIV. As with other infected individuals, $CD4^+$ lymphocyte counts and HIV titers are used to guide treatment regimens. Since 1985, in the manufacture of plasma-derived concentrates a triple barrier to viral contamination of plasma-derived concentrates has been employed: (1) self exclusion for donors, (2) donor screening with serologic tests for HIV, and (3) viral inactivation during concentrate production. Recombinant concentrates also are now widely

available. Acquisition of HIV-1 through factor concentrate in patients with hemophilia has been virtually nonexistent since 1985.

Viral Hepatitis

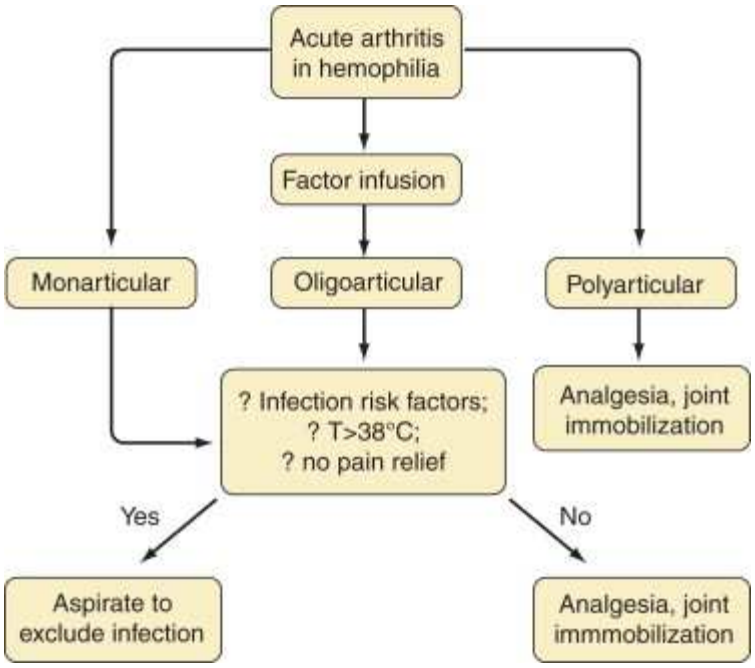
A second infectious side effect of either cryoprecipitate or factor concentrate is hepatitis, which may be a result of parenterally transmitted hepatitis A, B, C, or G virus; cytomegalovirus; or other as yet unidentified pathogens. In most series, most patients with hemophilia treated before the 1980s have plasma levels of hepatitis B virus surface antibody, and a few (2% to 5%) carry hepatitis B virus surface antigen. Approximately 80% of hemophiliacs transfused before 1990 have antibody to hepatitis C virus, [45] which, in contrast to hepatitis B virus antibody, is a marker for ongoing infection. Virucidal concentrate treatment methods have reduced, but not eliminated, parenteral transmission of hepatitis B and C viruses. Transmission of hepatitis A and G viruses also has been reported with the use of plasma-derived concentrates. Vaccination against hepatitis B and hepatitis A is now recommended for infants with hemophilia. Transmission of hepatitis has decreased dramatically because almost all pediatric patients are treated with recombinant products.

THERAPY FOR MUSCULOSKELETAL COMPLICATIONS OF HEMOPHILIA

Acute Haemarthrosis

The most important measure in therapy for acute haemarthrosis is prompt correction of the clotting abnormality by administration of the deficient factor. Arthrocentesis, if it is accomplished within 24 hours of the onset of symptoms (but after factor replacement), may be symptomatically beneficial in advanced acute haemarthrosis; however, for diagnostic and potentially therapeutic purposes, it should be considered mandatory at any time if suspicion of infection is high.[4, 7] Analgesia and brief joint immobilization for no more than 2 days often aid in pain control. Subsequently, passive range-of-motion isometric exercise should be initiated to reduce the likelihood of joint contracture.

Algorithm of acute arthritis in hemophilia.



Chronic Hemophilic Arthropathy

Conservative

A variety of conservative measures can bring remarkable benefit in the setting of chronic hemophilic arthropathy, [46 -49] including the following:

Prophylactic factor infusions

Intensive physical therapy for muscle building and increased joint stability

Periods of avoidance of weight bearing to allow regression of synovitis

Correction of flexion contractures by wedging casts, night splints, or the judicious use of traction

Training in sports to allow future maintenance of muscle mass

In modern treatment programs, aspiration of joints with chronic synovial effusions is rarely necessary or of lasting benefit. Failure of these conservative modalities to relieve symptoms or produce regression of synovitis should prompt consideration of other options, including local corticosteroid injections (which have been described as useful more recently),[50] the use of nonsteroidal anti-inflammatory drugs (NSAIDs), synovectomy, and joint replacement in the end stage.

Despite the obvious theoretical contraindications to the use of NSAIDs in hemophilia (i.e., the antiplatelet effects), several NSAIDs may be used safely for short periods as adjuncts to the conservative regimen. Ibuprofen, salsalate, and magnesium salicylate have been shown in a few patients to be safe and efficacious in reducing joint pain and analgesic dependence,[51,52] although long-term regression of synovitis and modification of the course of chronic hemophilic arthropathy have not been shown with any NSAID. The selective

cyclooxygenase-2 inhibitor class of NSAIDs does not have significant antiplatelet effects and theoretically should be safer than conventional NSAIDs in patients with hemophilia. Rofecoxib and valdecoxib have been withdrawn from the market because of a causative link to increased risk of cardiovascular events. Although others are in development, celecoxib, the only remaining cyclooxygenase-2 inhibitor on the market, has not been specifically tested in hemophilic patients and, similar to other NSAIDs, should be used with caution.

Synovectomy

Synovectomy in the setting of hemophilic arthritis has been shown to reduce the incidence of recurrent haemarthrosis and the severity of synovitis. This procedure can be accomplished surgically, arthroscopically, or through intra-articular injections of radioactive colloids. Patients should be considered for synovectomy if, despite aggressive conservative measures as outlined previously, persistent hemarthroses continue with ongoing chronic synovitis. In our center, specific indications for synovectomy include persistence of at least two hemarthroses per month in the same joint accompanied by symptoms and signs of chronic synovitis despite at least 4 months of conservative therapy, including intensive factor replacement. The major drawback to surgical synovectomy remains the observation, confirmed in most series,

[53,54] that joint motion is reduced postoperatively compared with preoperative baseline joint motion, despite intensive rehabilitation.

To overcome this finding and the high cost of hospitalization and factor replacement therapy attendant with surgical synovectomy, arthroscopic synovectomy has been employed in chronic hemophilic arthritis in recent years. Most follow-up series report that this technique is as successful as surgical synovectomy and results in less loss of motion,[55,56,57] particularly when continuous passive motion is used in the postoperative period.[58]The total cost of the procedure is less than that of surgical synovectomy, as is the rehabilitation period. Postoperative bleeding after arthroscopic synovectomy has been associated with poor results.

An alternative to surgical or arthroscopic synovectomy is ablation of the synovium using either radioisotopic or chemical agents, as reviewed more recently.[32,59,60] Such a nonoperative approach has been successful in reducing bleeding episodes by 70% to 80% in patients with hemophilia[61]and is especially useful in patients with circulating factor inhibitors, in whom surgery is relatively contraindicated. Commonly used radioisotopes in the United States include colloidal ^{23}P chromic phosphate, yttrium 90, and radioactive colloidal gold (^{198}Au). Theoretical long-term carcinogenic and teratogenic effects remain the major concerns associated with this technique in patients

who may have long life expectancies and are still of reproductive age; these effects have limited the use of radioisotopes in the United States, but less so in Europe. Chemical synovectomies using osmic acid, rifampicin, and hyaluronic acid have been attempted in some European centers with modest success, especially in children.[59] The short-term results of radioactive and chemical synovectomies are similar, although long-term outcomes may be superior in radioisotopic synovectomy.[32]Radioactive and chemical synovectomies remain experimental in the United States. Both have the advantages of being minimally invasive, requiring little factor replacement, and resulting in little morbidity, and both are much less expensive than operative procedures.

Total Joint Replacement

Major orthopaedic procedures, including total joint replacements, [62-65] have been employed safely and successfully in end-stage hemophilic arthropathy, including in patients with inhibitor antibodies.[66] The primary indication for total joint replacement is pain in an involved joint that is refractory to all conservative measures. Careful preoperative planning is imperative, including assessment for the presence of inhibitors, planning for factor replacement, and planning for a multidisciplinary rehabilitative program.[67] It is concerning, however, that most hemophilic patients in need of total joint replacement are young and may, if they are not infected with HIV, have a long life expectancy. If the procedure is

performed at a young age, this virtually ensures the need for one or more revisions during the patient's lifetime. In addition, patients are at increased risk for complications of surgery because of their underlying coagulopathy, and loosening is observed more commonly than in nonhemophilic patients in long-term follow-up. These findings suggest that total joint replacement should be reserved for the most severe cases of hemophilic arthropathy and deferred as long as possible. A comprehensive recent review details the many orthopaedic procedures that are now available for alleviating the pain and deformity resulting from hemophilic arthropathy.[68]

Dosing Regimens for Bleeding and Prophylaxis in Hemophilia

Site	Factor Level	Dose HemophiliaA	Dose HemophiliaB	Duration of Treatment	Comments
Joint	30%–70%	15–35 U/kg	30–70 U/kg	1–3 days	Splinting temporary splinting, no weight bearing
Life threatening (eg, intracranial, retropharyngeal, retroperitoneal)	80%–100%	40–50 U/kg	80–100 U/kg	10–14 days	Antifibrinolytic therapy with retropharyngeal bleeds
Soft tissue	30%–50%	15–25 U/kg	30–50 U/kg	2–5 days	Higher levels can be used for compartment

Site	Factor Level	Dose HemophiliaA	Dose HemophiliaB	Duration of Treatment	Comments
					syndrome
Surgery	80%–100%	40–50 U/kg	80–100 U/kg	10–14 (or shorter for minor procedures)	Significant blood loss can occur into large muscles of the lower extremity and the iliopsoas
Oral	20%–50%	10–25 U/kg	20–50 U/kg	1–2	Antifibrinolytic therapy
Gastrointestinal[*]	30%–100%	15–50 U/kg	30–100 U/kg	2–3	Should be evaluated for source
Genitourinary[†]	30%–50%	15–25 U/kg	30–50 U/kg	1–2	Avoid Antifibrinolytic therapy
Prophylaxis[‡]	50%	25 U/kg	50 U/kg	qod or 3?/week	Steroids may be useful

Data from DiMichele, Lusher, and Mannucci.

* Depending on severity.

† Painless spontaneous hematuria often requires no treatment other than fluid intake. Persistence requires treatment and evaluation.

‡ Use of a schedule of 25 U/kg qod and a dose of 40 U/kg with an interval of 2 days between the next dose may increase compliance by decreasing infusions to three per week.

MATERIALSAND METHODS

MATERIALS AND METHODS

This study was done at the haemophilia clinic and the medical wards of Coimbatore Medical College.

Fourty haemophilic patients already diagnosed as per factor assays and registered under haemophilic society of India, were included in the study.

INCLUSION CRITERIA

1. Patients above 15 years of age.

2. Presence of bleeding manifestations.

3. Consent of patient available for the study.

EXCLUSION CRITERIA

1. Patients less than 15 years of age.

2. Patients with no bleeding manifestations.

3. Consent not available.

SOURCE OF DATA

40 patients with haemophilia admitted in Coimbatore medical college during the study period from June 2010 to October 2011..

Haemophilic patients admitted without any bleeding manifestations were excluded from the study.

An informed consent was taken. The study protocol was approved by the Ethical Committee of Coimbatore Medical College Hospital.

The indications of admissions were noted. Also took a note of patients who had earlier admissions and indication of admission, then.

The patients were then subjected to both clinical and radiological evaluation for the early detection of haemophilic arthropathy.

Patients with no soft tissue and skeletal abnormalities were taken as normal. All the patients were then subjected to clinical examination and they were evaluated radiologically, either with CT/MRI of the knee joint by a qualified radiologist.

We used knee joint because it is the most common and earliest joint to get involved in haemophilic arthropathy. Haemophilic arthropathy of knee joint was graded as per Arnold-hilgartner classification.

Arnold-Hilgartner classification is a plain radiograph grading system for haemophilic arthropathy of the knee.

Stage 0: normal joint.

Stage I : no skeletal abnormalities, soft-tissue swelling is present.

Stage II : osteoporosis and overgrowth of the epiphysis, no cysts, no narrowing of the cartilage space.

Stage III : early subchondral bone cysts, squaring of the patella, widened notch of the distal femur or humerus, preservation of the cartilage space.

Stage IV : findings of stage III, but more advanced; narrowed cartilage space.

Stage V : fibrous joint contractures, loss of the joint cartilage space, extensive enlargement of the epiphyses with substantial disorganization of the joint.

This method is sensitive in detecting early arthropathic changes, easy to perform, minimally invasive and ensures patient compliance.

The data was analysed and conclusions drawn.

ANALYSIS OF RESULTS

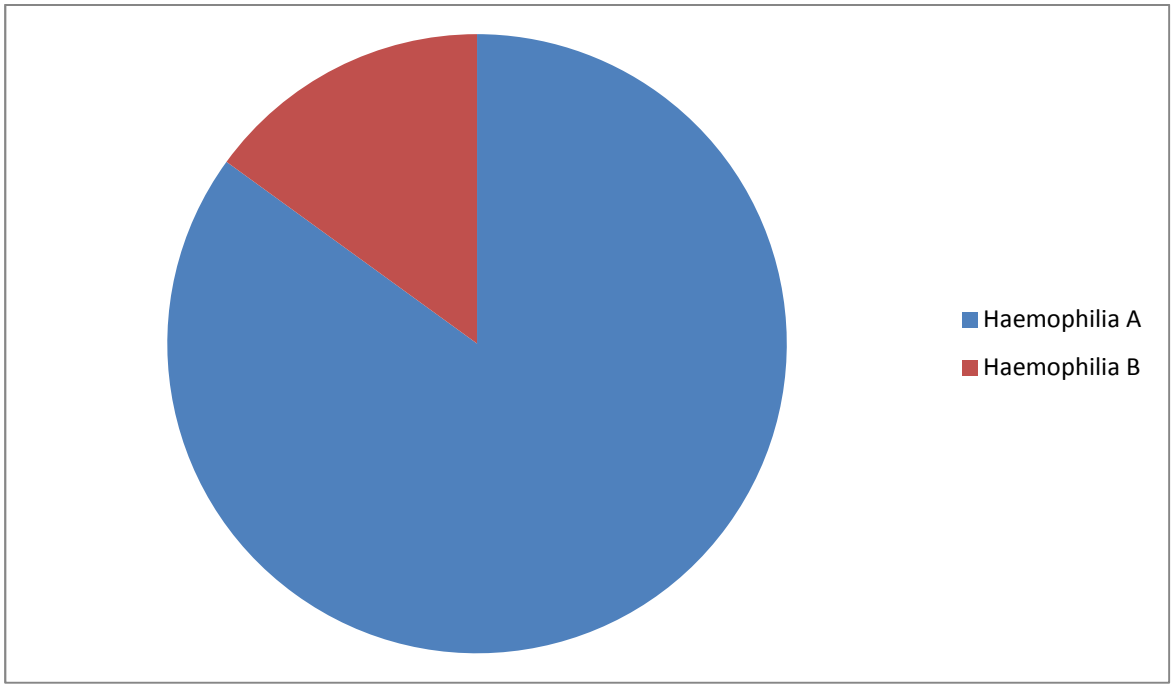
ANALYSIS OF RESULTS

A total of 40 patients were included in the study 39 males (97.5%) and 1 female (2.5%).

34 patients had haemophilia A and 6 of them were having haemophilia B. None of them had the rare haemophilia C.

Figure 1

PIE CHART SHOWING DISTRIBUTION OF HEMOPHILIA A AND B



The above chart shows that majority of cases in the study had hemophilia A

Age and sex distribution is shown in table no.1

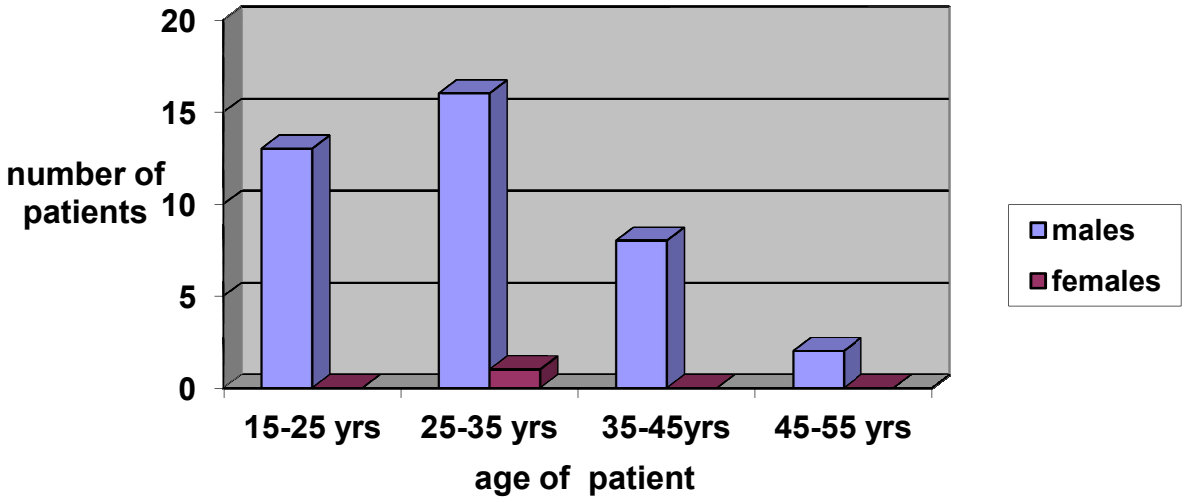
Table no.1 – TABLE SHOWING DISTRIBUTION OF PATIENTS BASED ON AGE AND SEX

Age group	sex			
	males	percentage	female	percentage
15-25 yrs	13	32.5	0	0
25-35 yrs	16	40	1	2.5
35-45 yrs	8	20	0	0
45-55 yrs	2	5	0	0

There was only a female patient in the study and she aged 25-35 yrs. Majority were males of age 25-35 yrs.

Figure 2

BAR DIAGRAM SHOWING DISTRIBUTION OF PATIENTS BASED ON AGE AND SEX



The above bar chart shows that majority of patients in the study were males.

Only one patient was a recently detected case of hemophilia (< 10 years) and a couple of patients were diagnosed for over 30 years. Majority of patients fell in the category where their diagnosis was made 10-30 years back.

Table no.2 –TABLE SHOWING DISTRIBUTION OF CASES BASED ON YEARS SINCE INITIAL DETECTION

Years after diagnosis	Number of patients	percentage
< 10yrs	1	2.5
10-20yrs	16	40
20-30yrs	21	52.5
>30yrs	2	5

In most of the patients initial diagnosis was made between 10 and 30 yrs of age.

Indications of admissions were assessed and most of them had musculoskeletal bleeds. Some got admitted due to ent bleeds, gi tract bleeds, cns bleeds, genitourinary and others in the decreasing order of frequency. It is given in following table.

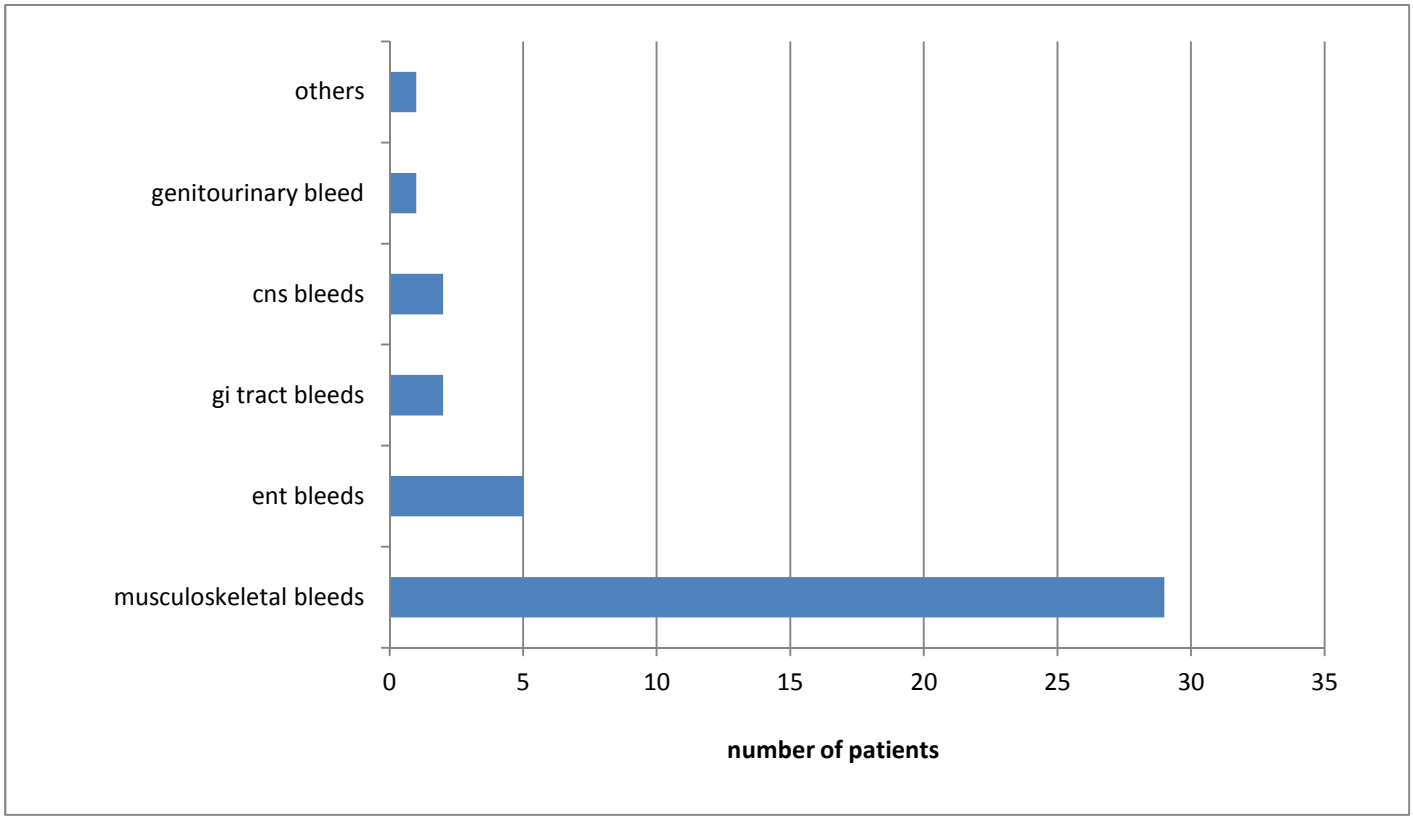
Table 3 – TABLE SHOWING INDICATIONS FOR IN PATIENT CARE OF HAEMOPHILIC PATIENTS

Indication for admission	Number of cases	percentage
Musculoskeletal bleed	29	72.5
Ent bleed	5	12.5
Gi tract bleed	2	5
Cns bleed	2	5
Genitourinary bleed	1	2.5
Others	1	2.5

The main indication of admission was for musculoskeletal bleeds.

Figure 3

BAR DIAGRAM SHOWING DISTRIBUTION OF CASES BASED ON INDICATIONS FOR INPATIENT CARE

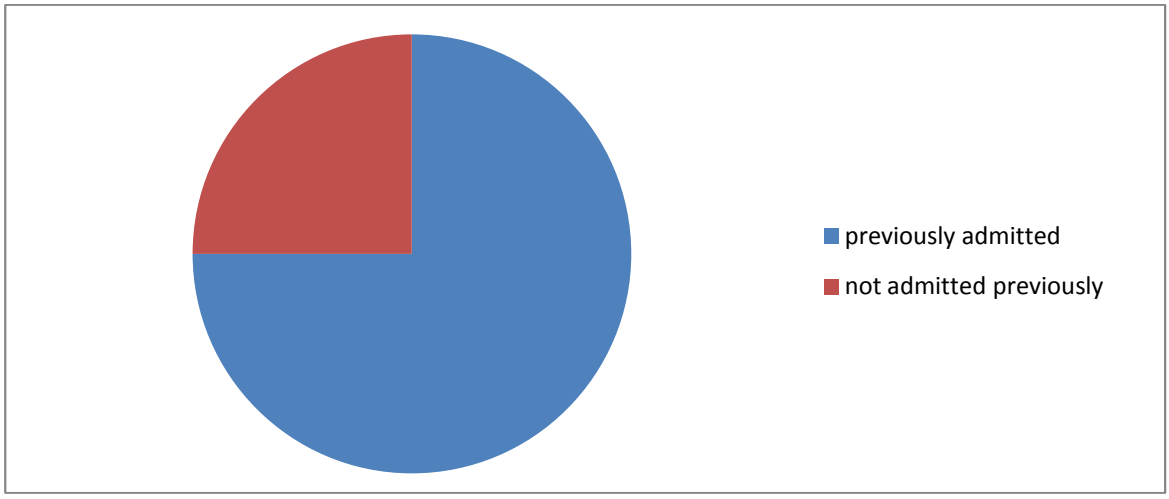


The above diagram shows that most of patients were admitted with musculoskeletal bleeds.

30 out 40 patients were previously admitted due to bleeding manifestations especially due to musculoskeletal bleeds. In fact 26 of these admissions were for that only

Figure 4

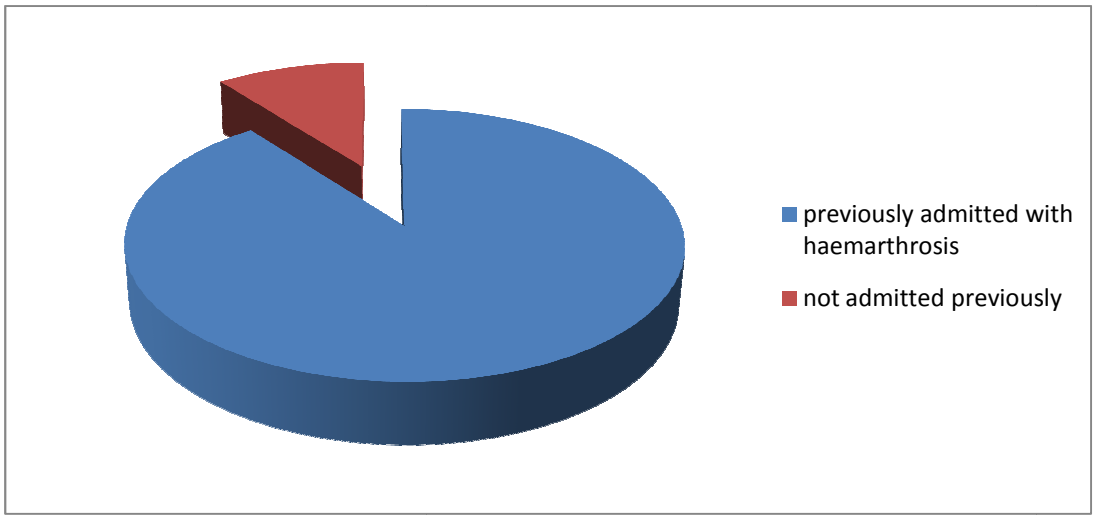
DIAGRAM SHOWING DISTRIBUTION OF CASES BASED ON PREVIOUS ADMISSION FOR BLEEDS



The pie chart shows that 75% of patients had history of inpatient care for bleeds in the past.

FIGURE 5

CHART SHOWING PATIENTS WHO WERE ADMITTED WITH RECURRENT MUSCULOSKELETAL BLEEDS

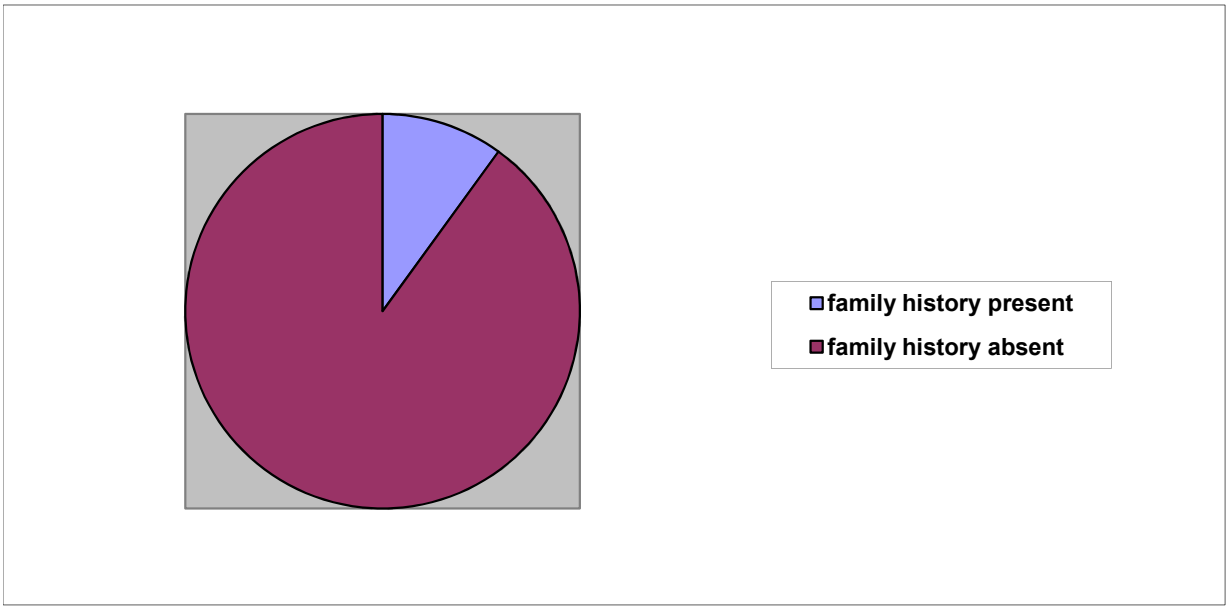


From the above chart we can see that 26 patients had recurrent haemarthrosis.

Family history was present in 10% of patients- 4 out of 40 cases studied

Figure 6

DIAGRAM SHOWING DISTRIBUTION OF PATIENTS BASED ON PRESENCE OF FAMILY HISTORY OF HEMOPHILIA



The above chart shows only few patients had positive family history.

All admitted patients were then subjected to clinical examination to assess the joint involvement, irrespective of whether they were admitted for haemarthrosis or not. Tests were done for joint mobility and stability and any swellings either soft tissue or bony were noted and recorded in the proforma prepared. Also looked for the presence of local warmth and tenderness of the joint.

After thorough clinical examination all 40 patients were subjected to radiological examination of both knee joints, as knee is the most commonly involved joint by

hemophilic arthropathy. Majority of patients also underwent CT/MRI of knee joint, especially those with either current or previous haemarthrosis. Then with the help of the qualified radiologist joint pathology was categorized into various stages as per the Arnold-Hilgartner classification.

The following table gives the staging of patients based on radiology

Table-4

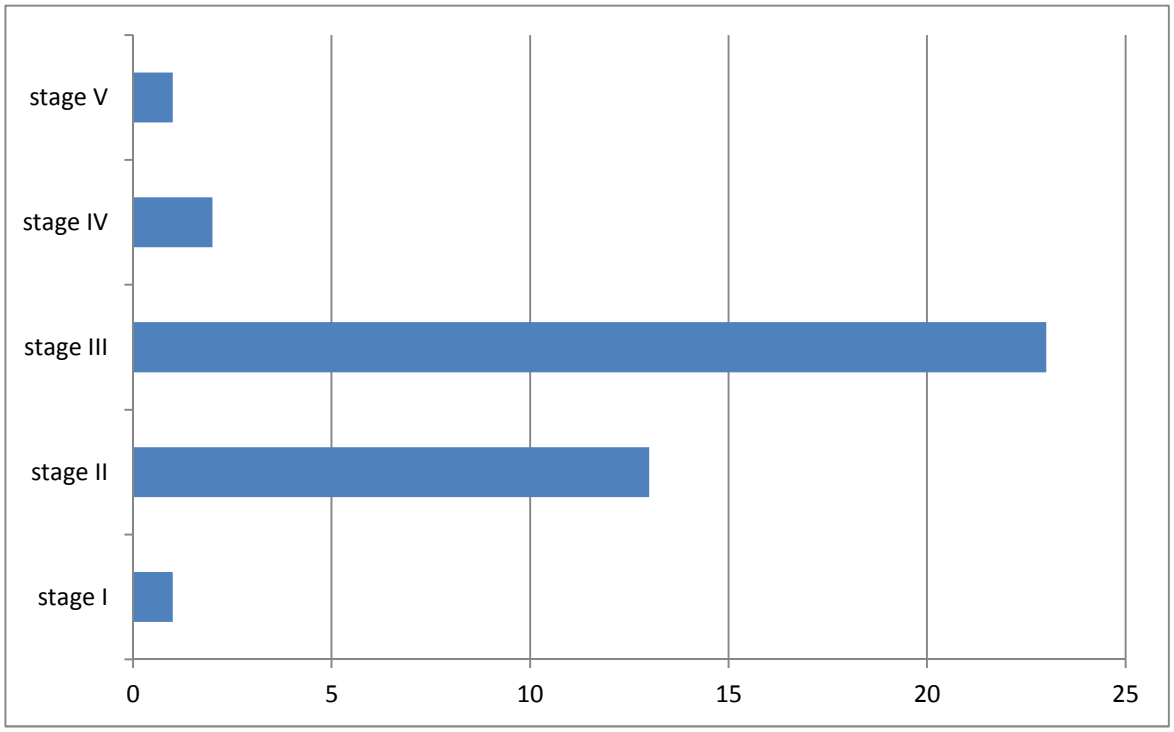
TABLE SHOWING DISTRIBUTION OF PATIENTS BASED ON FINDINGS IN RADIOGRAPHS OF KNEE BY ARNOLD –HILGARTNER CLASSIFICATION

Staging of joint	Number of patients	Percentage
I	1	2.5
II	13	32.5
III	23	57.5
IV	2	5
V	1	2.5

Majority of patients were in stage III, 23 out of 40 which accounts for 57.5% of study population.

Figure 7

DIAGRAM SHOWING DISTRIBUTION OF PATIENTS BASED ON FINDINGS IN RADIOGRAPHS OF KNEE JOINT BY ARNOLD - HILLGARTNER CLASSIFICATION



The above bar diagram shows that majority of cases had intermediate stages of involvement of knee joint

In patients with previous history of admission for musculoskeletal bleeds by way of clinical and radiological assay, we were able to quantify the arthropathy clearly. This helped both in patient education about the disease and also in management.

Up to stage III disease in which there is no articular cartilage damage, patients can be managed conservatively.

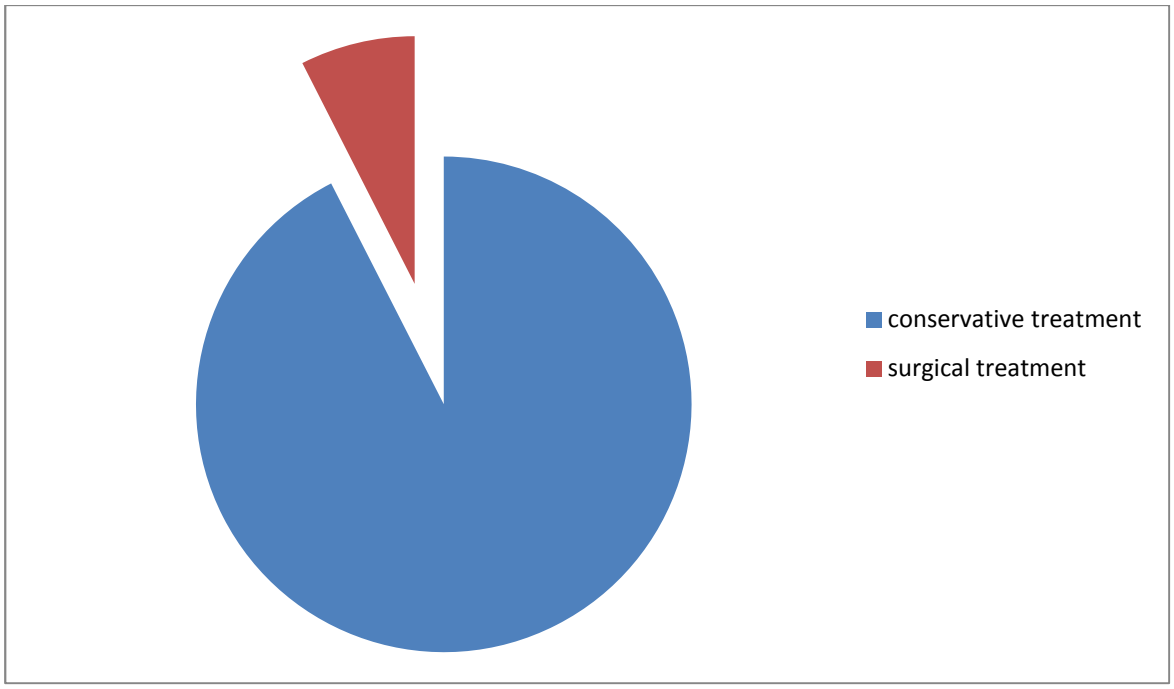
CT and MRI were suggested to those with stage III and above to have a look in to the finer details of the joint pathology. In almost all cases the findings of X-rays were consistent with that of CT/MRI. Early changes of hemophilic arthropathy can thus be detected with the help of CT/MRI.

But in those with advanced stages of arthropathy, only solution to prevent permanent damage to the joint was joint replacement therapy under factor cover. Three of the patients with advanced hemophilic arthropathy were referred to the orthopaedician for decision regarding joint replacement. CT and MRI of the joints were taken and assessed the severity and two patients underwent joint replacement surgery and one is awaiting confirmation for surgery.

Those with stage III and below were managed conservatively with factor replacement therapy based on body weight, analgesics and supportive measures like ice pack application. They were advised to follow up periodically on an out patient basis for early detection of worsening of arthropathy. Also highlighted the warning symptoms of the disease which requires admission like headache, bleed in to joint, muscle, or bleed from oropharynx, haematuria, haematemesis, hemoptysis etc

Figure 8

DIAGRAM SHOWING TREATMENT GIVEN IN CASES DETECTED



The above chart shows the most patients had conservative management.

We also noted the fact that if the duration of disease is more, the chance of developing advanced stage of disease is also more. Only one patient was recently diagnosed and he had a joint arthropathy grading of I. But those with long duration of disease more than 20 years and those on poor follow up were having advanced arthropathy when compared to those with regular follow up.

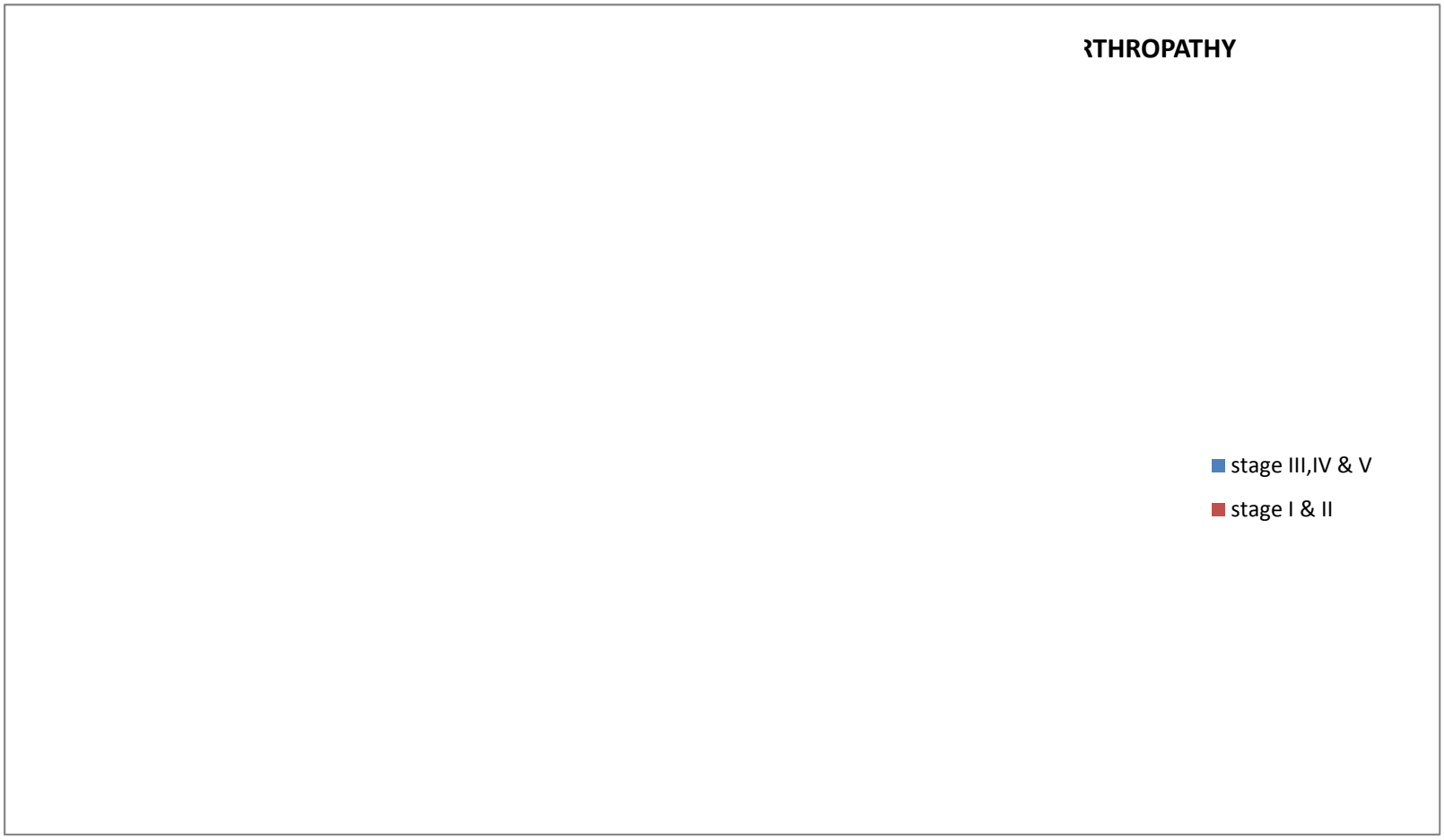
DISCUSSION

DISCUSSION

As arthropathy is the commonest complication faced by a haemophiliac patient, its early detection holds the key for his or her's better quality of life. Haemophilia almost always affects males and poses problems in their reproductive age group.

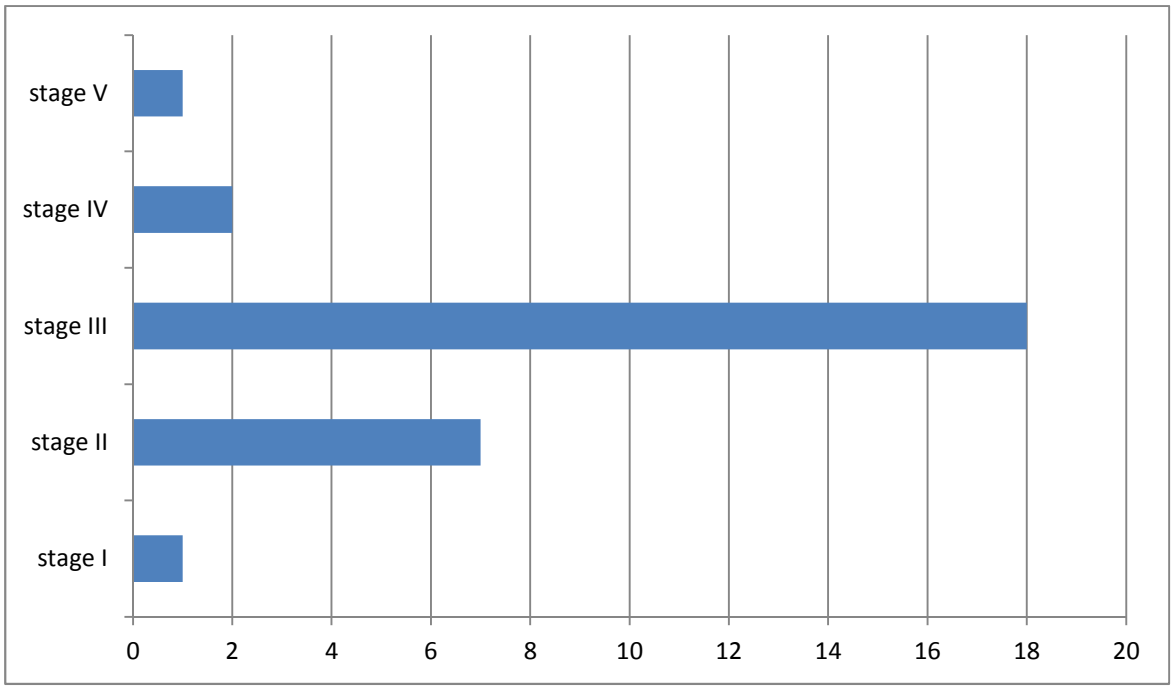
As suggested by James V. Luck etal.[69] the most common clinical manifestation of hemophilia is arthropathy secondary to recurrent hemarthroses and chronic synovitis. 72.5% of patients in our study were admitted for haemophilic arthropathy itself and rest with ent, gi tract, cns and other bleeds in the decreasing order of frequency.

Fred.f.ferry et al. [70] suggested that prophylaxis with recombinant factor VIII can prevent joint damage and decrease the frequency of joint and other hemorrhages in patients with severe haemophilia disease. This also points out the need for early detection, admission of patients and treatment with factor replacement therapy. In our study 29 patients got admitted with musculoskeletal bleeds out which 18 (62.07%) were in staging III of haemophilic arthropathy classification. Only two and one patients were categorized in the advanced stages IV and V respectively. Rest all patients were in lower stages which needed prompt treatment with factor replacement therapy and supportive care to halt the progression to advanced stages.



As shown in these diagrams late arthropathy was more common among the cases studied

FIGURE SHOWING STAGES OF HEMOPHILIC ARTHROPATHY IN CASES STUDIED



Out of 11 patients admitted with non musculoskeletal bleeds 10 of them clinically gave us no evidence of arthropathy. Remaining one patient had clinical arthropathy and stage III of haemophilic arthropathy. Out of the ten patients with no clinical evidence of arthropathy four were already in stage III of haemophilic arthropathy. So silently the have progressed to stage III without any symptoms and signs.

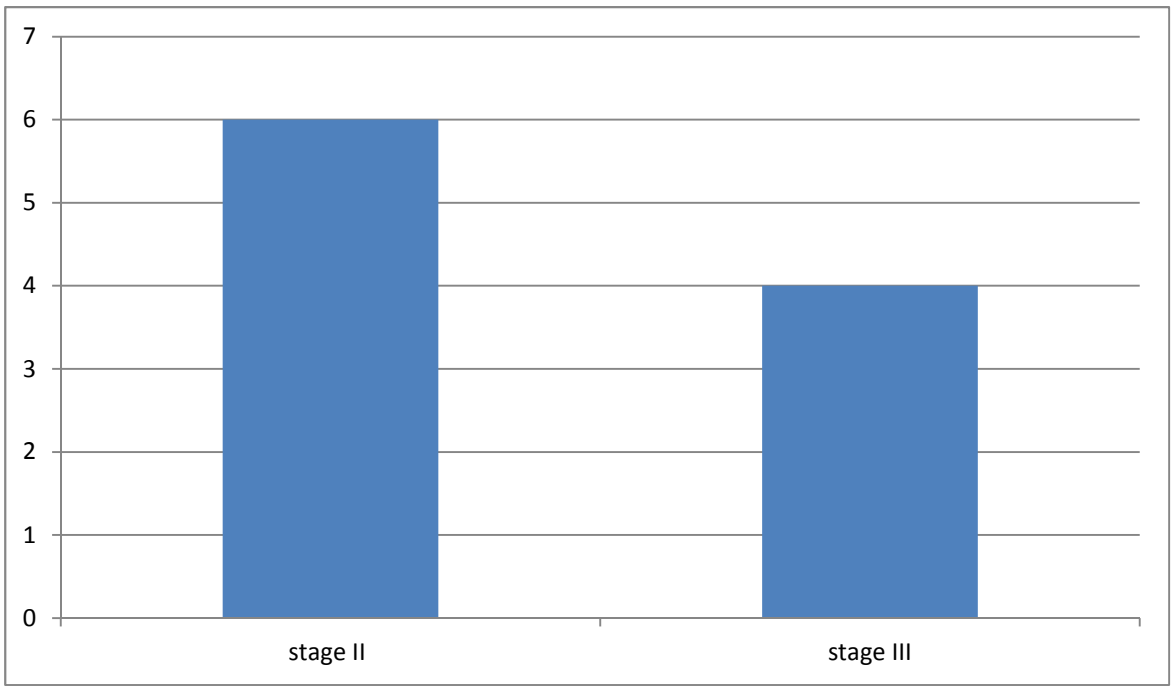


DIAGRAM SHOWING DISTRIBUTION OF HEMOPHILIC ARTHROPATHY DETECTED RADIOLOGICALLY

The management depends on the staging of arthropathy. Up to stage III conservative management is tried. According to v.krislo et al. the most common surgical procedures[71] used to manage hemophilic arthropathy are synovectomy, joint debridement, fusion, and joint arthroplasty. Arthroplasty and latest joint replacement therapy are reserved for those with permanent damage to the joint. In our study also we managed majority of patients conservatively and only 3 patients with severe joint damage and disfigurement were referred for orthopaedic procedures.

In our study we came to know the fact that as the duration of disease process is more, the risk of acquiring advanced stages of disease are more. Those with advanced stages of disease invariably had joint deformities despite adequate medical attention. As per Allen g, aledort etal.in end stage [72]haemophilic arthropathy if adequate measures are not undertaken, the joint will almost certainly progress to endstage arthropathy, which is best managed by surgery (ie, total arthroplasty for knees and hips or arthrodesis in ankles). So two of our patients underwent surgery – joint replacement and one is awaiting confirmation.

CONCLUSION

CONCLUSION

Haemophilia is a common coagulation disorder encountered by physicians. Males are almost always affected with very few exceptions. Haemophilia A is the one much more common than Haemophilia B. Haemophilia C is a rare coagulation disorder.

The most common indication for admissions are musculoskeletal bleeds and knee being the commonest joint involved. Iliopsoas is the major muscle involved with this kind of bleed. Other bleeds like ent bleeds, gi tract bleeds, cns bleeds etc.can all occur in haemophiliacs. As the duration of disease process increases the risk of permanent joint damage also goes on the increase.

The patients should be adequately educated about the disease. All patients with bleeding manifestations are treated with factor replacement therapy. All patients have to be screened periodically for early detection of arthropathy. Arthropathy staging is done as per Arnold hilgartner method.

Those patients with early stages of arthropathy are treated conservatively with factor replacement therapy to halt the progression of disease. If not treated adequately, due to chronic synovitis permanent joint damage occurs. Once this happens only surgical cure is possible to restore the joint function. The various

modalities available are synovectomy, arthroplasty and joint replacement in severe cases.

Even in haemophilics admitted for non-musculoskeletal indications arthropathy may lie undetected and if unnoticed can result in joint damage. So evaluation is needed noy only clinically but also radiologically as radiology detects it earlier.

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BIBLIOGRAPHY

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APPENDIX

MASTER CHART

Name	Age	Sex	Ip no.	Musculoskeletal bleed	Ent bleed	Git bleed	Cns bleed	Genitourinary bleed	Others	Duration of disease	Previous admissions	Clinical findings	Radiologic staging
Rajkumar	18	m	62123	y						b	y	n	III
Ravikumar	24	m	63007	y						b	y	n	III
Nagarj	34	m	63122		y					c	y	y	III
Abdul rahim	36	m	64190	y						c	y	y	III
Vasudevan	26	m	64298		y					b	y	n	II
Suresh	38	m	65289	y						c	y	y	III
Palanisamy	39	m	68004	y						c	y	y	III
Dinesh	16	m	005	y						a	n	n	I
Balasubramanian	29	m	178	y						c	y	n	III
Abdul rahman	19	m	274				y			b	n	n	II
Aruchamy	44	m	543	y						c	y	y	V
Lakshmi	28	f	678	y						c	y	y	III
Tyagarajan	26	m	741	y						b	y	n	II
Veerapandi	27	m	900	y						b	y	n	II
Senthil	19	m	902	y						b	n	n	II
Vinayakan	18	m	1378		y					b	n	n	II
Arumukam	46	m	1702			y				d	n	n	III
Govindraj	27	m	1890	y						c	y	n	III
Arusamy	33	m	2196	y						c	y	y	III
anwar	32	m	2278	y						c	y	n	III
Cristopher	48	m	2666		y					d	y	n	III
Sankar	38	m	2790	y						c	y	y	III
Ilangovan	18	m	3002	y						b	y	n	II
Marimuth	19	m	3713	y						b	y	n	II
Kandasami	26	m	3902	y						b	y	n	II
Palanisami	42	m	4123	y						c	y	y	IV
Rajasekar	43	m	5510			y				c	n	n	III
Sekar	29	m	6129	y						c	y	y	III
Prakasam	30	m	6782	y						c	y	n	III
Bharath	18	m	7921					y		b	n	n	II
Vivek	19	m	8829						y	b	n	n	II
Arunachalam	28	m	9921	y						c	y	y	III
Vadivel	27	m	9929	y						c	y	y	III
Murugan	31	m	10019				y			c	n	n	II
Murali	40	m	10789	y						c	y	y	IV
Raj	24	m	12105	y						b	y	n	III
Sakthivel	23	m	13290	y						b	y	n	III
Sreedhar	31	m	14920		y					c	y	n	III
Anbalagan	20	m	16002	y						b	n	n	II
Saravanan	32	m	17003	y						c	y	y	III

PROFORMA

PROFORMA

Name: Age / Sex:

Address:

DOA: DOD:

Chief complaints

1. Duration of bleeding
2. Onset of bleeding
3. Site involved
4. Pain or discomfort
5. Precipitating event
6. Progression of bleeding
7. History suggestive of complication like headache, abdominal pain

Past history

1. H/O DM / HTN
2. H/O TB
3. H/O Surgery
4. H/O previous admission and its indication
5. H/O of factor or blood transfusion

Family history

1. H/O DM / HTN
2. H/O TB
3. H/O of haemophilia

Personal history

1. Diet
2. Sleep
3. Bowel / Bladder
4. Smoker / Alcoholic

GENERAL PHYSICAL EXAMINATION

1. Obese / Not Obese
2. Nutritional status: Poor / Avg / Good
3. Pallor
4. Icterus
5. Cyanosis / Clubbing
6. General – Lymphadenopathy
7. PR
8. BP

Local examination

Depending on the site of bleeding

Examination ok knee joint

Inspection

1. gait
2. attitude
3. swelling
4. muscular wasting

Palpation

1. local rise of temperature
2. local tenderness
3. swelling
4. popliteal fossa
5. bony compartments
6. wasting
7. joint

Movements

Flexion and extension
Abduction and adduction
Rotation

Measurements

Length of the limb
Inter malleolar separation

ABBREVIATIONS

ABBREVIATIONS

HIV – Human Immunodeficiency Virus

MRI – Magnetic Resonance Imaging

CT – Computed Tomography

FFP – Fresh Frozen Plasma

PCCs – Prothrombin Complex Concentrates

EACA – Epsilon Amino Caproic Acid

DDAVP – 1-Deamino 8- D Arginine Vasopressin

rFVIIa – Recombinant Activated Factor VII

CNS – Central Nervous System

GIT – Gastro Intestinal Tract

ENT – Ear Nose Throat

NSAIDs – Non Steroidal Anti-inflammatory Drugs

CPPD – Calcium Pyrophosphate Deposition Disease

RA – Rheumatoid Arthritis

OA – Osteo Arthritis

CONSENT FORM

CONSENT FORM

Yourself Mr/Mrs/Ms……..…… are being asked to be a participant in the research study titled "**A STUDY OF HAEMOPHILIC PATIENT'S INDICATION FOR ADMISSION AND EARLY DETCTION OF ARTHROPATHY**" in CMC Hospital, Coimbatore, conducted by Dr.Unnikrishnan.S., Post Graduate Student in the Department of General Medicine, Coimbatore Medical College. You satisfy eligiblility as per the inclusion criteria. You can ask any question you may have before agreeing to participate.

Research Being Done

Indication of admission and early detectionof haemophilic arthropathy in Coimbatore Medical College

Purpose of Research

- To find the indications of admissions in haemophilia patients.
- To detect haemophilic arthropathy at an early stage with clinical and radiological testing.

Procedures involved

The research includes detailed clinical examination including medical history, physical examination with reference to the indication of admission. Physical examination involves examination of knee joint based on movements and measurements. Then radiology of the knee joint is done for all patients and staging of arthropathy done. Only in patients with advanced staging CT/MRI of the knee joint may be taken.

Decline from Participation

You have the option to decline from participation in the study existing protocol for your condition.

Privacy and Confidentiality

Privacy of individuals will be respected and any information about you or provided by you during the study will be kept strictly confidential.

Authorization to publish Results

Results of the study may be published for scientific purposes and/or presented to scientific groups, however you will not be identified.

Statement of Consent

I volunteer and consent to participate in this study. I have read the consent or it has been read to me. The study has been fully explained to me, and I may ask questions at any time.

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Signature /Left thumb impression Date

(volunteer)

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Signature of witness Date